A
n accurate diagnosis built on history, physical examination, and testing is the critical first step in successful management of epilepsy and isolated seizures in children. Determining the risk for recurrence is, of course, the paramount concern to both clinician and parents. In the United States, the estimates of recurrence risk range from 23% to 71%, with most of the variation in estimates attributable to study design and distribution of prognostic factors.¹ In a recent large study, only one third (33%) of children with single unprovoked seizures had recurrences within 5 years.²

Thus, the early full evaluation of the seizure disorder often provides the evidence base to reassure parents. And for those children in whom recurrent events are deemed likely, classifying the epileptic complex by clinical, etiologic, and electroencephalographic (EEG) findings provides the necessary framework for ongoing evaluation and long-term treatment.

Because an initial seizure can present in such varied settings, and because the majority of new-onset cases in children will actually yield no identifiable cause, no single diagnostic strategy will apply to evaluation of all children. This review will summarize a flexible and evolving diagnostic approach that is appropriate for the pediatric patient with presumptive epilepsy. An evaluation built on a basic history and a simple testing algorithm as described here should help neurologists avoid unnecessary tests while still constructing a full diagnosis of the syndrome that allows for accurate prognosis and successful therapeutic choices.³

HISTORY

A child’s first seizure prompts a host of questions: Is it really a seizure? Was the onset focal? Is central nervous system dysfunction or a metabolic precipitant evident? What is the likely seizure type or syndrome type? What diagnostic studies are required and which, if any, antiepileptic drugs (AEDs) should be started?

Discovery of the key historic features (Table 1) is the main guide in answering these important questions. Because children often cannot provide first-hand accounts of their seizures, much of this history is necessarily second- or third-hand, such as what a parent reports or what a mother says that the teacher, grandparent, or babysitter witnessed.

Knowing how seizure history relates to recurrence risk can guide the clinician’s initial evaluation. For example, contrary to our earlier understanding, nei-
ther the age at the time of first seizure nor the duration of the seizure (eg, presentation with status epilepticus) seem to be associated with increased risk of recurrence. Recurrences, if they do occur, tend to occur early, with about half striking again within 6 months and more than 80% within 2 years.\(^1,2,4-6\)

**Etiology** is another strong predictor of recurrence, with remote symptomatic seizures recurring at a higher rate than idiopathic events (68% versus 37% at 6.3 years in one study).\(^3\) These remote symptomatic seizures have various causes, including major head trauma, previous central nervous system (CNS) infection, stroke, and static encephalopathy (such as mental retardation or cerebral palsy).

Sleep state and seizure type may also correlate with increased risk for recurrence. In one study of 407 children, those awake at the time of seizure had a recurrence risk of 36% compared to a risk of 53% for those with seizures during sleep (Table 2).\(^5\) Other studies have shown that a slight but inconsistently higher recurrence rate may occur with partial seizures.\(^1\) Family history does not seem to play a role in the remote symptomatic group, but genetic risk may affect the likelihood of seizure recurrence in the idiopathic group.

### LABORATORY TESTS

In addition to obtaining the history and performing physical and neurologic examinations, a variety of tests are available for evaluation of new-onset seizures. These include chemistries (eg, electrolytes and metabolic screens), hematologic tests, and assays for infectious agents present in the cerebrospinal fluid (CSF), blood, or urine. These tests are generally tailored to the individual situation. Specifically, electrolytes may be valuable only in patients with emesis, diarrhea, or who have suspected dehydration. Patients with an underlying endocrine or renal condition or who are younger than 12 months of age may also be at higher risk for potentially treatable electrolyte abnormalities. A toxin screen is appropriate in all cases of unexplained seizures and metabolic or chromosomal studies are typically ordered to investigate developmental delay or other suspect findings.

Analysis of CSF is most often considered when CNS infections, such as meningitis or...
encephalitis, are suspected. It may also be appropriate in children with febrile seizures who are younger than 12 to 18 months or as an elective part of the metabolic workup for children of any age.

**Routine EEGs**

The main neurophysiologic tests are the EEG, the ambulatory EEG, and the video EEG. Imaging technologies employed most often include the anatomic tests such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound and the functional tests such as functional MRI, positron emission tomography (PET), and single photon emission computed tomography (SPECT).

Although some of these tests will be critical in specific instances (see **Special Considerations: Neonatal Seizures**), the basic EEG provides the testing cornerstone for epilepsy diagnosis. An EEG should be ordered in all first seizures except perhaps cases of simple febrile seizure. The wide-ranging utility of the EEG in this setting is clear (Table 3), and the American Academy of Neurology now recommends EEG as part of the routine neurodiagnostic evaluation of the child with an apparent first unprovoked seizure.7

How sensitive is the EEG in the diagnosis of epilepsy? In 1 study of 429 adults with definite epilepsy, a single EEG demonstrated interictal epileptiform discharges (IEDs) in 50% of cases.8 By the fourth serial recording, 92% of patients had displayed IEDs.

In addition to providing the important information listed in Table 3, an abnormal initial EEG also can predict an increased likelihood of recurrence, especially in those with idiopathic seizures.9 Although most studies indicate that EEGs are predictive of recurrence, the details of these findings vary. For example, one study indicates that only IEDs in patients with generalized seizures are associated with an increased risk of recurrence9 while another study shows that the recurrence rate increases with IEDs in both focal and generalized seizures.7

**Long-Term EEG Monitoring**

Monitoring via ambulatory EEG or laboratory-based video EEG can increase the likelihood of detecting epileptiform discharges, aid in the quantification of seizure burden, and capture behaviors allowing for more accurate diagnosis. Certain syndromes, such as pseudoepilepsy, may only be diagnosed using such longer-term EEG recordings.

A recent study of ambulatory EEG in 84 children and adolescents with diagnosed or suspected epilepsy...
clarifies the potential value of ambulatory EEG. While a major point of the study was to evaluate the utility of digital analysis of ambulatory EEG in children, the overall value of the EEG in the assessment of seizures in children is also underscored. Over the course of 1.4 days, ambulatory EEG recorded epileptiform activity in 73% and 86% of those with confirmed (n=49) or suspected (n=35) epilepsy, respectively, while routine EEG demonstrated epileptiform activity in only 45% and 17% of these groups, respectively. Also, the seizure diagnosis and classification based on the ambulatory EEG findings matched the initial diagnosis in only 19% of the cases. For example, while the original impression was that 75% had generalized epilepsy, the new data indicated that only 21% of these cases had generalized epilepsy. Overall results were discordant in 63% of cases. Thus, the prolonged EEG technique offered additional accuracy in the classification of seizures in selected pediatric patients. The ability to detect more events and to record these events with higher accuracy allows the clinician to fashion a more appropriate workup, classification, and treatment approach.

Video EEG may be the procedure of choice for documentation of pseudoseizures, events that superficially resemble seizures but lack the characteristic clinical and EEG features. This long-term monitoring may also aid in the diagnosis of so-called EEG-negative seizures, in correlation of EEG and clinical events, and localization before focal resection. Because partial simple seizures may have a scalp EEG correlate in only about 15% of patients and because seizures arising from mesial parasagittal, or orbital frontal regions frequently are undetectable when using routine scalp recordings, the video EEG, especially when scalp electrodes are employed, offers the only option for neurophysiologic evaluation.

**NEUROIMAGING**

Neuroimaging techniques (Table 4) are used in pediatric neurology to find developmental malformations (eg, focal cortical dysplasias), vascular malformations, destructive lesions, neurocerebrovascular lesions, degenerative disorders (eg, Krabbe’s disease), metabolic disorders, inflammatory or infectious conditions, and hippocampal lesions.

Although cranial ultrasound allows real-time bedside studies in unstable patients (eg, infants during the perinatal period), definitive diagnosis usually requires CT or MRI. When it was first introduced about 20 years ago, radiographic CT revolutionized imaging of the CNS, and most institutions today still rely on CT scans for rapid and relatively low-cost image generation. However, neurologists now generally acknowledge several weaknesses of the traditional CT. These include: potential for contrast reaction, radiation exposure, bony artifact in middle fossa, and inability to image mesiotemporal sclerosis and migrational disorders.

Currently, the imaging study of choice is the MRI. In fact, anatomic imaging (MRI preferred) should be obtained in all symptomatic partial and generalized epilepsies. An MRI is also appropriate if a CT is normal or if the clinical picture progresses. Imaging is not necessary in well-defined epilepsy syndromes such as childhood absence or benign epilepsy with centrotemporal spikes.

For separating gray from white matter (eg, focal cortical dysplasias) T1-weighted images are best. For assessing white matter abnormalities and temporal lobe abnormalities, T2-weighted images are preferred. Fluid-attenuated inversion recovery (FLAIR) can help distinguish lesions from CSF while gadolinium-enhanced images can improve the yield in T1-weighted images when lesions have produced the breakdown of the blood-brain barrier.

A recent review of CT and MRI in children with epilepsy showed that neuroimaging has, in general, been useful in select populations. Out of 9 class I or II studies reviewed, 223 of 1290 cases imaged (17.3%) exhibited...
ed some abnormality. The main findings in those studies involving CT or MRI included atrophy, infarction, evidence of trauma, cerebral dysgenesis, and cortical dysplasia. In most studies, MRI was consistently more sensitive than CT in picking up abnormalities.

A similar review of neuroimaging in children with newly diagnosed epilepsy found etiologically relevant abnormalities in 62 of 488 imaged cases. The authors concluded that neuroimaging should be especially helpful in children with neurologic deficits, partial seizures, or focal EEG abnormalities that were not part of an idiopathic localization-related epilepsy syndrome.

In coming years, several variations on the MRI may become more important in daily practice, including the following:

- Quantitative magnetic imaging can detect subtle unilateral or bilateral hippocampal volume loss and also correlates with neuronal loss in the hippocampus.
- Magnetic resonance spectroscopy measures specific brain metabolites, and may eventually be valuable in detecting epileptic foci (e.g., 31P spectroscopy showing an abnormal ratio of phosphocreatine to inorganic phosphate, or 1H spectroscopy showing abnormalities in N-acetylaspartate, creatine, and choline).
- Magnetic resonance relaxometry can demonstrate abnormalities seen in up to 80% of T2-weighted images (compared to 50% to 65% normally) in patients with temporal lobe epilepsy.

Similarly, functional MRI is not required for the vast majority of epilepsy patients. In most cases, these special techniques are reserved for presurgical evaluations. For example, because it employs extremely rapid scanning to detect changes in blood flow, functional MRI can detect seizure foci during events. A number of groups are investigating the use of functional MRI to lateralize speech and motor function before surgery.

A variety of markers such as 2-deoxy-2-fluoro-D-glucose are available for PET studies. Interictal analysis can demonstrate regional hypometabolism in the epileptogenic zone, but these PET changes are typically more extensive than those seen during MRI or EEG tests. The role of PET in extratemporal epilepsy is less clear, but the technique may eventually assist in directing intracranial electrode placement.

Finally, ictal SPECT is quite accurate in detecting both temporal and extratemporal lobe epilepsy via changes in blood flow. One investigator found positive ictal scans in 91% of children with frontal lobe epilepsy. Accuracy of SPECT depends on the timing of injection, however, it is crucial that the injection occur early in the course of the seizure as defined by the EEG.

**QUESTIONS & ANSWERS**

Children are commonly referred with EEGs interpreted as showing epileptiform abnormalities. On closer inspection, many of these EEGs show normal variant patterns that mimic seizure-like patterns. Do such misinterpreted EEGs ever confuse the typical evaluation?

**Dr. Morton:** Yes, commonly misinterpreted variants include the phantom 6-Hz spike and benign epileptiform transients of sleep. The normal variants are very common in preschool children, and that’s why we need to read EEG interpretations from institutions less familiar with children with caution.

Should children with benign Rolandic epilepsy who do not respond to appropriately administered pharmacotherapy be imaged with MRI?

**Dr. Duchowny:** In my experience, pediatricians refer virtually all of their patients with a first seizure to a neurologist. If it’s anything more than a febrile seizure, the anxiety level in the pediatrician or the family...
builds rapidly. They are quite motivated to quickly refer patients to pediatric neurologists.

Dr Morton: Yes, any patient who begins to deviate from a well-described benign course—and I would say nonresponsiveness to a first medication qualifies here—should be investigated with imaging.

When should general practitioners or neurologists refer patients to centers for full evaluations perhaps even using techniques such as video EEG telemetry?

Dr Morton: Again, prolonged monitoring is most appropriate for those children who deviate from the course anticipated based on the history and diagnosis. This may include, for example, those with intractable disease who have an anatomic abnormality or who have failed to be controlled after 2 or 3 medications. These are often focal resection candidates or they require clarification of seizure type, so they may benefit from the video unit. In other cases, such as developmental abnormalities or in evaluating non-convulsive seizure versus medication effect, the prolonged monitoring may not be necessary.

Are standard EEGs underutilized as a basis for diagnosis?

Dr Morton: The EEG is invaluable in making the diagnosis but we need to remember that the clinical symptomatology in some cases may supersede the EEG in significance. In other situations, we may also be underutilizing more sophisticated tools, such as video EEG. In patients with nocturnal epileptic events, for example, EEG and ambulatory EEG are frequently normal. Only the video monitoring will allow you to make this diagnosis.

Dr Lesser: But the tools for evaluation must be employed selectively. In certain cases, for example in suspected frontal lobe epilepsy, the standard EEG will quite properly drive the diagnostic evaluation.

REFERENCES